

## **REMARKS**

### **Status of the Claims**

Claims 1-4, 6, 7 and 10 are pending. Claims 1-4, 6, 7 and 10 are rejected. Claim 1 is amended.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendments. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

### **Amendments to the claims**

Claim 1 is amended to overcome the rejection of claims 1 - 3 under 35 U.S.C. §112, second paragraph. No new matter has been added.

### **The 35 U.S.C. §112, second paragraph rejections**

Claims 1, 2 and 3 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses the rejection.

The Examiner states that claims 1 and dependent claims 2-3 are vague and indefinite in that claim 1 recites "an animal in need of such treatment," because it is not clear which animal is in need of such treatment.

Claims 1-3 were amended by removing the limitation "in need of such treatment". Accordingly, the Applicant respectfully requests that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

The 35 U.S.C. §102(b) rejections

The rejection of claims 1 and 4 under 35 U.S.C. 102(b) as being anticipated by **Fuks et al.** (1994) was maintained for reasons set forth in the office action mailed on 27 February 2002. Applicant respectfully traverses the rejection.

The Examiner states that **Fuks** teaches that the administration of basic fibroblast growth factor (b-FGF) to an animal leads to the inhibition of radiation-induced endothelial cell death (endothelial apoptosis). Thus, although **Fuks** does not expressly teach that the administration of basic fibroblast growth factor leads

to the inhibition of the generation of ceramide from sphingomyelin, this is an inherent property of the administration of basic fibroblast growth factor that cannot serve as a basis of patenting that process. Therefore, according to the Examiner, it does not matter whether **Fuks** teaches or suggests a different mechanism of action, and thus **Fuks** anticipates claims 1 and 4.

The Applicant maintains that **Fuks** does not anticipate claim 1. **Fuks** teaches that administration of basic fibroblast growth factor to an animal inhibits radiation-induced endothelial apoptosis. Amended claim 1 recites a method of inhibiting the generation of ceramide from sphingomyelin, comprising the step of administering basic fibroblast growth factor to an animal. In contrast to claim 1, **Fuks** does not teach, either expressly or inherently, that administration of basic fibroblast growth factor to an animal inhibits the generation of ceramide from sphingomyelin. The Applicant contends that disclosure of a particular compound in the prior art does not provide a proper basis for rejection of a method claim that encompasses a previously undisclosed function of the compound, even though the function may be inherent in the structure of the compound. It is well established that an Applicant may seek patent protection for a new use of a known compound.

The Applicant also maintains that **Fuks** does not anticipate claim 4, for the same reasons argued above. In addition, unlike claim 4, **Fuks** does not teach the administration of basic fibroblast growth factor as a method to treat endotoxic shock or any other disease. The data in **Fuks** demonstrate that *in vitro*, basic fibroblast growth factor down-regulates apoptosis such that a greater percentage of cells survive at the lower radiation doses applied (see Figure 1). **Fuks** also states that the ability to increase cell survival at such a dose range is of interest because it corresponds to those commonly used in the management of human tumors (see Discussion, page 2586). **Fuks** contemplates that basic fibroblast growth factor administration may serve as a radioprotective agent *in vivo* that may have important clinical implications relevant to clinical radiotherapy, making it possible to actively intervene in specific pathways to favorably alter the therapeutic ratio in the radiation treatments of several types of human cancer (see Discussion, page 2589). Therefore, **Fuks** aims to provide a way to increase the survival of normal cells in radiation treatments in order to allow the use of higher therapeutic radiation doses, thus improving the ratio of killing of cancer cells versus normal cells. **Fuks** makes no teaching that basic fibroblast growth factor could be used as a therapeutic

treatment for radiation damage, or that it could be used as a treatment for sepsis or endotoxic shock. Therefore, because **Fuks** does not teach all of the elements of claim 4, claim 4 is not anticipated by **Fuks**.

Accordingly, considering the above arguments, Applicant respectfully requests that the rejection of claims 1 and 4 under 35 U.S.C. §102(b) be withdrawn.

Claim 10 stands rejected under 35 U.S.C. §102(b) as being anticipated by **Fuks et al.** (1994). Applicant respectfully traverses this rejection.

The Examiner states that **Fuks** teaches a method of administering basic fibroblast growth factor (b-FGF) into an animal to inhibit radiation-induced programmed cell death *in vitro* and *in vivo*. Instant claim 10 is drawn to a method of treating sepsis by administering basic fibroblast growth factor. Therefore, **Fuks** anticipates instant claim 10, because it teaches the administration of basic fibroblast growth factor into an animal. The administration of basic fibroblast growth factor would inherently lead to the inhibition of ceramide generation from sphingomyelin, and would lead to the

treatment of sepsis, because a product's function is an inherent property of its structure.

For the same reasons as argued above, the Applicant maintains that **Fuks** does not anticipate claim 10. **Fuks** does not teach administration of basic fibroblast growth factor as a method of treating an individual at risk for sepsis; therefore, **Fuks** does not teach all the elements of claim 10 and so does not anticipate claim 10. Accordingly, Applicant respectfully requests that the rejection of claim 10 under 35 U.S.C. §102(b) be withdrawn.

The 35 U.S.C. §102(a) rejection

Claims 1, 4 and 10 are rejected under 35 U.S.C. §102(a) as being anticipated by **Hamivotiz-Friedman et al.** (December 1, 1997). Applicant respectfully traverses this rejection.

Applicant points out that the date of publication of the Hamivotiz-Friedman reference is December 1, 1997. The instant application claims the benefit of priority of provisional U.S. Serial no. 60/066,286 filed November 20, 1997. The priority date of the instant application precedes the date of publication of the **Hamivotiz-Freidman** reference; therefore, this reference is not a valid prior art reference under 35 U.S.C. §102(a). Accordingly, the

Applicant respectfully requests that the rejection of claims 1, 4 and 10 under 35 U.S.C. §102(a) be withdrawn.

The 35 U.S.C. §103(a) rejection

Claims 1-4, 6 and 7 stand rejected under 35 U.S.C. §103 as being unpatentable over **Fuks et al.** (1994). Applicant respectfully traverses these rejections.

The Examiner states that although **Fuks** does not disclose a method of administering basic fibroblast growth factor to an animal using the doses and times recited in claims 3 and 7, **Fuks** does teach a method of administering basic fibroblast growth factor to an animal to inhibit radiation-induced endothelial apoptosis. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to design a method of administering basic fibroblast growth factor to a human and to optimize both the dosage and duration of said administration to get the benefits of this protein, because many pathological conditions such as endotoxic shock lead to endothelial apoptosis.

Applicant respectfully submits that claims 1, 4, 6 and 7 are patentable over **Fuks et al.**, because **Fuks** contains no suggestion that would motivate one skilled in the art to arrive at the

instant invention. Amended claim 1 recites a method of inhibiting the generation of ceramide from sphingomyelin comprising the step of administering basic fibroblast growth factor to an animal. Claim 4 recites a method of treating endotoxic shock in an animal by administering basic fibroblast growth factor to said animal. Dependent claim 6 provides that said animal is a human. Dependent claim 7 provides a dosage range and timing for basic fibroblast growth factor. Similarly to the arguments presented above under 35 U.S.C. §102(b), **Fuks** teaches the administration of basic fibroblast growth factor to prevent apoptosis in endothelial cells sensitive to radiation-induced killing, and suggests that such administration could improve the efficacy of radiation therapy for the treatment of cancer. **Fuks** contains no suggestion that basic fibroblast growth factor could be used as a therapeutic agent for the treatment of any disease. In addition, even if one skilled in the art could be motivated by **Fuks** to attempt to develop basic fibroblast growth factor administration as a treatment for a disease, this motivation rises to the level of being “obvious to try” and it is well established that “obvious to try” is not the correct standard for determining obviousness under 35 U.S.C. §103. Applying the function of basic fibroblast growth factor to the development of a treatment for a

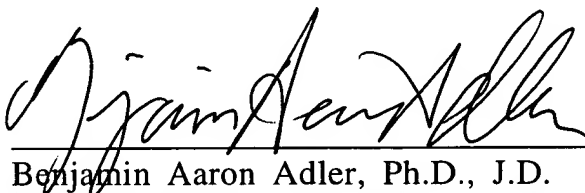
disease, such as a treatment for endotoxic shock, requires one skilled in the art to go beyond any teaching or suggestion encompassed by **Fuks**. At a minimum, arriving at the claimed methodology after a reading of the teachings of **Fuks** would involve an undue amount of experimentation. Therefore, claims 1, 4, 6 and 7 are patentable over **Fuks**. Accordingly, Applicant respectfully requests that the rejection of claims 1, 4, 6 and 7 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed July 2, 2002. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date:

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

Please amend claim 1 as follows:

1. (twice amended) A method of inhibiting the generation of ceramide from sphingomyelin comprising the step of administering basic fibroblast growth factor to an animal ~~in need of~~ such ~~treatment~~.